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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,342	09/18/2000	Rudi Brands	01975.0025	8325
22852 7590 05/07/2008 FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413			EXAMINER FORD, ALLISON M	
			ART UNIT 1651	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/582,342	Applicant(s) BRANDS, RUDI	
	Examiner ALLISON M. FORD	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>20080222</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's reply of 22 February 2008 has been received and entered into the application file. Claims 1-38 have been cancelled, and new claims 39-44 have been presented. Claims 39-44 are the only claims pending in the current application, all of which have been considered on the merits. All arguments have been fully considered, and will each be addressed below, as appropriate. Rejections not repeated herein have been withdrawn.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 371, which papers have been placed of record in the file. Additionally, acknowledgment is made of applicant's claim for foreign priority based on PCT/EP98/08522 filed on 17 December 1998, which further claims priority to Dutch application 97204110.7 filed on 24 December 1997. A certified copy of the foreign priority application is present in the instant application file.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Applicants' arguments against the rejection previously of record have been fully considered, but are not found persuasive.

Applicants have argued that reliance on the technique of sourdough bread production is non-analogous to the invention of the current invention, which deals with cell culture. As such, Applicants

Art Unit: 1651

submit that one would not have been able to predict the results of using the method of splitting and passing on portions of the sourdough starter in the technique of preparing cells for production of biologicals.

In response, it is respectfully submitted that sourdough starter is actually a cell culture, and therefore is relevant to the art of cell culture, in at least as far as it pertains to methods of propagating a cell culture. Furthermore, it is submitted that the discussion of sourdough friendship bread was only relied upon to show the extreme commonness of the idea of 'repeated discontinuous' processes of culture. Still further, it has been held that "[W]hen a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability." See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) at 1396. Thus, even if one were to interpret propagation of sourdough starter culture as being non-analogous to cell culture, modifications and variations to improve methods can be imported across different fields of art.

Applicants have further argued that the absence of clear anticipatory teachings in the art is evidence of long-felt need which is met only by the current invention.

In response, it is respectfully submitted that Applicants have not established a long-felt need. Establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution. The relevance of long-felt need and the failure of others to the issue of obviousness depends on several factors. First, the need must have been a persistent one that was recognized by those of ordinary skill in the art. *In re Gershon*, 372 F.2d 535, 539, 152 USPQ 602, 605 (CCPA 1967) ("Since the alleged problem in this case was first recognized by appellants, and others apparently have not yet become aware of its existence, it goes without saying that there could not possibly be any evidence of either a long felt need in the . . . art for a solution to a problem of dubious existence or

Art Unit: 1651

failure of others skilled in the art who unsuccessfully attempted to solve a problem of which they were not aware."); *Orthopedic Equipment Co., Inc. v. All Orthopedic Appliances, Inc.*, 707 F.2d 1376, 217 USPQ 1281 (Fed. Cir. 1983) (Although the claimed invention achieved the desirable result of reducing inventories, there was no evidence of any prior unsuccessful attempts to do so.). Furthermore, the instant case is considered to be a situation where the concept of the invention was, in fact, so well known, that specific disclosure of such in written protocols was generally unnecessary. Skilled artisans recognize that to continuously produce a desired biological product in culture, the culture must be continually tended to, maintained and replenished when exhausted, due to the need to replenish, a stock started culture would routinely be maintained.

A prima facie case of obviousness has been made over the instant claims, Applicants have not successfully rebutted such to demonstrate non-obviousness.

Claims 39-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (Scale-up of Suspension and Anchorage-Dependent Animal Cells in Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, pp.59-75). The discussion of the history of "Amish Friendship Bread" pulled from <http://recipecircus.com> ("Friendship Cake/Bread History") and <http://en.wikipedia.org> ("Amish Friendship Bread") are also relied upon in this rejection to establish the definition and recipe of the bread recipe which calls for a starter culture.

Griffith et al disclose methods for preparing culture of anchorage-dependent cells for the production of biological products, the details of which have been made of record previously. Generally, Griffith et al disclose inoculating cells onto a substrate, such as a roller bottle (solid support) or microcarrier beads (particulate matter), culturing the cells until they reach confluence, removing the culture media, adding trypsin to the cell culture to release the cells from the substrate, then passaging the

Art Unit: 1651

cells. It is noted the initial cell culture of Griffith et al reads on what Applicants are calling the 'preproduction batch', the passaged cells read on what Applicants are calling the 'production batch'.

Griffith et al differ from the instant invention only in that, while they disclose splitting and passaging the cells of their 'preproduction batch', they do not specifically disclose a first portion of the cells are replated as a seed for a subsequent 'preproduction batch', and a second portion of the recovered cells are transferred and used as a 'production batch' specifically for the production of biological products, which Applicants are calling a 'repeated discontinuous process'.

However, it is maintained that replating a portion of the cells as a seed for subsequent 'preproduction batches', and transferring a second (larger) portion of cells for use as a 'production batch' for production of biological products produced by the cells (*i.e.* performing a repeated discontinuous process), would have been routinely performed by one of ordinary skill in the art, and therefore the invention is held to be *prima facie* obvious. The concept of splitting a culture, using the majority of it for production of a biological product, and retaining and maintaining smaller portion as a seed culture is a routine method in the art. Due to the fact that such is so well known, it is not routinely included in written protocols intended for artisans of ordinary skill. To exemplify its commonplace in the art, processes for production of sourdough or "Friendship Bread" (See, for example, "Friendship Cake/Bread History" from <http://recipecircus.com> (accessed 8/6/2007), or the discussion at Wikipedia under "Amish Friendship Bread" (accessed 8/6/2007)) is cited. Production of sourdough bread involves dividing of a starter culture into two portions, using one portion for the production of the bread, and sharing the other portion with a friend, wherein the friend can repeat the process; in such a manner single cultures can exist for years.

One of ordinary skill in the art would have been motivated to retain and reseed at least one portion of the culture as a seed for future 'preproduction batches' in order to continue the cell line, thereby saving money (by not needing to purchase a subsequent cell culture seed), and increasing the amount of

Art Unit: 1651

biological product which can ultimately be produced (as the initial culture is not exhausted after the first round of biological product production, but a small portion can be retained, passaged and expanded, so as to provide a cell source for future 'production batches'). One would have had a reasonable expectation of successfully carrying out this 'repeated discontinuous process' because the steps of splitting and passaging cell cultures, as well as steps for obtaining biological products from a 'production culture' were well known in the art (see, e.g. Griffith et al), and are even regularly carried out by non-skilled artisans (such as in the process of passing on sourdough starter cultures).

Therefore, the instantly claimed method is not considered to be patentable, as it was obvious to one of ordinary skill at the time the invention was made. One would have known how to culture anchorage-dependent cells to produce a biological product, as illustrated by Griffith et al and it would be well within the purview of the skilled artisan, and generally common sense, to maintain a portion of the cell culture during each split, to replenish the original culture and use to repeat the process, thereby prolonging the culture life and increasing the amount of culture which can be used to produce the desired product.

It is further pointed out that this rationale relies on common sense and the knowledge generally available to the skilled artisan must be taken into account; such may be taken into consideration as rationale for rendering an invention patentable per the Supreme Court decision of *KSR International Co vs. Teleflex Inc.* Specifically, the Supreme Court held that "Variations of particular work available in one field of endeavor may be prompted by design incentives and other market forces, either in same field or different one, and if person of ordinary skill in art can implement predictable variation, 35 U.S.C. §103 likely bars its patentability; similarly, if particular technique has been used to improve one device, and person of ordinary skill would recognize that it would improve similar devices in same way, then using that technique is obvious unless its actual application is beyond person's skill, and court resolving obviousness issue therefore must ask whether improvement is more than predictable use of prior art

Art Unit: 1651

elements according to their established functions.” See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) at 1386.

Finally, with regards to the production of viruses as the specific biological product, it is noted that the methods of Griffith et al and Pollard et al are applicable to all anchorage-dependent cell types. Furthermore, anchorage-dependent cells that are routinely cultured to product viruses are also known in the art. For example, MDCK cells are notoriously old and well known in the art for their use in culture to grow viruses (dating back to at least the 70s). Therefore it would have been obvious at the time the invention was made to split and passage MDCK cells, per the repeated discontinuous culture process discussed above for the production of viruses.

Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1651

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALLISON M. FORD whose telephone number is (571)272-2936. The examiner can normally be reached on 8:00-6 M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651